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SEMINAR ON BALLOON AORTIC VALVULOPLASTY—IV

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Patient Age and Results of Balloon Aortic Valvuloplasty: The Mansfield Scientific Registry Experience

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Patients enrolled in the Mansfield Scientific Aortic Valvuloplasty Registry were followed up a mean of 7 months after balloon aortic valvuloplasty. Results were compared for patients <70, 70 to 79 and ≥80 years of age at time of valvuloplasty. As assessed by aortic valve area indexed to body surface area, stenosis was more severe in the older patients and the incidence of congestive heart failure was also greater in those aged ≥80 years.

The results of valvuloplasty were comparable in all three age groups, and indexed final valve area was not significantly different among the groups. In-hospital mortality ranged from 4.2% to 9.4%, but this and other complications were not significantly different among the groups. Total 7 month mortality was 23%. As performed in this registry study, balloon aortic valvuloplasty produced similar results in older and younger patients, despite initially more severe disease in the older patients.

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Balloon aortic valvuloplasty has been used for palliation of aortic stenosis in selected patients who for various reasons are poor candidates for aortic valve surgery (1–12). Although usually applied in the frail elderly patient, this technique also has been used in younger patients who have coexistent severe noncardiac disease. Other investigators (13) have reported that the results of balloon aortic valvuloplasty may be better in younger than in older patients. Indeed, this concept has encouraged some centers to advocate performance of balloon aortic valvuloplasty as a primary procedure in younger patients (14). Although many factors undoubtedly determine immediate and long-term outcomes of balloon aortic valvuloplasty, one hypothesis is that younger patients may have less advanced aortic valve disease, allowing larger increases in valve opening and final aortic valve area.

The purpose of this investigation is to compare the results of valvuloplasty in younger versus older patients in the Mansfield Scientific Aortic Valvuloplasty Registry.

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Methods

The Registry. The Mansfield Scientific Aortic Valvuloplasty Registry comprises data prospectively collected from 27 participating centers involved in the performance of aortic balloon valvuloplasty. Data forms from each center were provided for each patient undergoing balloon aortic valvuloplasty at that center and these were sent to Mansfield Scientific for collation and statistical analysis. At initial evaluation, baseline clinical and laboratory data were recorded on each individual, including measurements made at cardiac catheterization and before and after balloon aortic valvuloplasty. Follow-up was performed by clinician visits and telephone interviews at 3 month intervals.

Data analysis. In order to compare results in patients of different age(s), the patient(s) were divided into three groups: those < 70 years of age, those 70 to 79 years of age, and those ≥80 years of age. Successful valvuloplasty was defined as an increase in valve area of ≤25%, or a decrease in pressure gradient of ≥50%, or both, in surviving patients not requiring aortic valve replacement during hospitalization. End points for immediate results included aortic valve area and peak systolic gradient, procedural complications and mortality. Follow-up end points included need for aortic valve replacement or repeat valvuloplasty, mortality and functional class. All patients had at least one 6 month

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Table 1. Baseline Characteristics of Patients <70, 70 to 79 and ≥80 Years of Age Undergoing Balloon Aortic Valvuloplasty

	<70 Years	70 to 79 Years	≥80 Years	p Value
N (total = 492)	59	168	265	
Women (%)	34%	52%	63%	p < 0.001
Age (yr) (mean ± SD)	62.4 ± 8.8	75.5 ± 2.7	84.3 ± 3.5	p < 0.001
Valve area (cm^2)	0.61 ± 0.22	0.52 ± 0.19	0.47 ± 0.16	p < 0.001
Valve area index* (cm^2/m^2)	0.34 ± 0.09	0.31 ± 0.11	0.29 ± 0.11	p < 0.01
Valve gradient (mm Hg)	55.2 ± 23.8	59.8 ± 22.3	60.8 ± 23.5	NS
Cardiac output (liters/min)	4.5 ± 1.7	4.1 ± 1.3	3.6 ± 1.1	p < 0.001
Cardiac index (liters/min per m^2)	2.65 ± 0.83	2.37 ± 0.75	2.26 ± 0.75	p < 0.005
Aortic regurgitation (no. of pts.; %†)				
None	11; 30%†	28; 29%†	52; 38%†	
Mild	20; 54%†	59; 61%†	71; 51%†	
Moderate	6; 16%†	10; 10%†	15; 11%†	NS
N/A	22	71	127	

*For valve area indexes, n = 47, 140 and 232, respectively, for the three groups. †These percents indicate the total number of patients who had aortography performed, not the total study group. N/A = data not available; pts. = patients.

follow-up evaluation with mean follow-up time of slightly >7 months.

Statistical analysis. Differences in baseline characteristics and outcome variables were assessed among the three patient age groups. Statistical significance was determined by one-way analysis of variance and the chi-square test. Average values within groups were expressed as mean values ± SD. Valve areas were expressed as absolute values with correction for body surface area. Univariate and discriminant analyses were performed for selected variables in each age group in order to determine primary predictors of survival at follow-up.

Results

Baseline clinical characteristics (Tables 1 to 3). Baseline characteristics for the 492 patients undergoing balloon aortic valvuloplasty in the Mansfield Registry are shown in Table 1. Fifty-nine patients were <70 years of age at the time of valvuloplasty, 168 were 70 to 79 years of age and 265 were ≥80 years of age. The proportion of female to male patients increased in the older age groups ($p < 0.005$). Of patients ≥80 years of age, 63% were female, almost twice as great as the percent of female patients <70 years of age.

For each age group, valve area decreased with increasing

Table 2. Angiographic and Functional Baseline Characteristics of Patients <70, 70 to 79 and ≥80 Years of Age Undergoing Balloon Aortic Valvuloplasty

	<70 Years	70 to 79 Years	≥80 Years	p
Coronary arteriography (no. of pt.; %*)				
≥50% stenosis (≥1 vessel)	22; 44%*	61; 43%*	107; 50%*	NS
N/A	9	27	51	
Pts. with >50% stenosis				
1 vessel	5; 10%*	26; 18%*	44; 21%*	
2 vessel	7; 14%*	12; 9%*	29; 13%*	NS
3 vessel	10; 20%*	22; 16%*	33; 15%*	
Pts. with LMCA	2; 4.0%*	3; 2.1%*	8; 3.7%*	
NYHA class (no. of pts.; %†)				
I	1 (2%†)	6 (4%†)	11 (5%†)	NS
II	11 (21%†)	27 (17%†)	25 (11%†)	
III	18 (34%†)	78 (50%†)	106 (45%†)	
IV	23 (43%†)	45 (30%†)	92 (39%†)	
N/A	6	12	31	

*Percents are of the total number of patients with coronary arteriography performed (n = 50, 141, 214, respectively, for the three groups); †percent of the total number of patients with New York Heart Association classification (n = 53, 156, 234, respectively); ‡ comparison of classes I and II vs. classes III and IV. LMCA = left main coronary stenosis >50%; other abbreviations as in Table 1.

Table 3. Clinical and Procedural Baseline Characteristics of Patients <70, 70 to 79 and ≥80 Years of Age Undergoing Balloon Aortic Valvuloplasty

	<70 Years	70 to 79 Years	≥80 Years	p Value
Baseline symptoms (no. of pts. present pts. assessed)				
Fatigue	37/54 (69%)	113/154 (73%)	153/227 (67%)	NS
Dyspnea	53/58 (91%)	149/162 (92%)	225/248 (91%)	NS
Angina	31/57 (54%)	92/161 (57%)	120/251 (48%)	NS
Syncope	10/56 (18%)	33/170 (19%)	57/240 (24%)	NS
CHF	35/53 (66%)	85/148 (57%)	169/226 (75%)	p = 0.002
Technique (no. of pts.)				
Single balloon	40 (68%)	122 (73%)	191 (72%)	
Double balloon	19 (32%)	45 (27%)	74 (28%)	NS
Largest OD ≤20 mm	32 (54%)	108 (64%)	166 (63%)	
Largest OD >20 mm (includes double)	27 (46%)	60 (36%)	99 (37%)	

CHF = congestive heart failure; OD = outer balloon diameter; other abbreviations as in Table 1.

age ($p < 0.001$). Because of the increasing proportion in the larger groups of women with presumably smaller body surface area, valve area was normalized for body surface area, creating a valve area index. As expected, the valve area index also decreased with increasing age, from 0.34 ± 0.09 cm^2/m^2 in patients <70 years, 0.31 ± 0.11 cm^2/m^2 in those 70 to 79 years and 0.29 ± 0.11 cm^2/m^2 in those ≥80 years of age ($p < 0.01$). Peak systolic valve gradient measured at catheterization ranged from 55 to 60 mm Hg and was not substantially different among the three groups. Both cardiac output and cardiac index decreased significantly with increasing patient age. The presence and severity of aortic regurgitation did not differ substantially among the three age groups.

Coronary arteriography was performed in a similar majority of patients in all three groups (Table 2). There were no significant differences in numbers of patients with single, double and triple vessel coronary disease.

Table 2 also demonstrates the New York Heart Association functional class; the majority of patients in each group were in functional classes III and IV. Likewise, there were no statistically important differences in the prevalence of fatigue, dyspnea, angina and syncope among the three groups of patients (Table 3). Congestive heart failure was more common in patients aged ≥80 years ($p = 0.002$). Most patients (>68% in each group) underwent single balloon valvuloplasty (p = NS) and the largest balloon size (≤20 mm) was used in most patients (54% to 64% in the three groups; p = NS).

Immediate results of balloon aortic valvuloplasty (Table 4). The success rate ranged from 83% to 89% and was not significantly different among the groups. The final valve area (cm^2/m^2) after valvuloplasty was inversely related to patient age, averaging 0.9 ± 0.34 in patients <70 years of age, 0.84 ± 0.32 in patients 70 to 79 years of age and 0.79 ± 0.31 in patients ≥80 years of age ($p < 0.05$). However, when these values were normalized for body surface area, there were no

Table 4. Immediate Results of Balloon Aortic Valvuloplasty

	<70 Years	70 to 79 Years	≥80 Years	p Value
Success* (no. of pts.)	49/63 (77%)	144/165 (87%)	236/265 (89%)	NS
Final valve area (cm^2)	0.90 ± 0.34	0.84 ± 0.32	0.79 ± 0.31	p < .05
Final valve area index (cm^2/m^2)	0.53 ± 0.15	0.50 ± 0.20	0.50 ± 0.21	NS
Increase in valve area (cm^2)	0.32 ± 0.22	0.32 ± 0.23	0.33 ± 0.21	NS
Increase in valve area index (cm^2/m^2)	0.17 ± 0.16	0.19 ± 0.15	0.20 ± 0.17	NS
Final valve gradient (mm Hg)	28.8 ± 12.6	30.3 ± 13.2	29.0 ± 14.5	NS
Decrease in valve gradient (mm Hg)	−26.5 ± 17.5	−29.4 ± 16.9	−31.5 ± 17.7	NS
Final cardiac index (liters/min per m^2)	2.74 ± 0.82	2.50 ± 0.82	2.42 ± 0.89	p < .001
Complications† (no. of pts.)				
None	45 (76%)	138 (82%)	208 (78%)	NS
One	7 (12%)	20 (12%)	40 (15%)	NS
Two	6 (10%)	8 (5%)	16 (6%)	NS
Three or more	1 (2%)	2 (1%)	1 (0.4%)	NS
In-hospital deaths	5 (8.5%)	7 (4.2%)	25 (9.4%)	NS

*Success is defined as ≥25% increase in valve area or a ≥50% decrease in pressure gradient, or both, and no death or valve replacement during the in-hospital period; †not including death. Abbreviations as in Table 1.

Table 5. Outcome at Last Follow-Up*

	<70 Years (N = 59)	70 to 79 Years (N = 168)	≥80 Years (N = 265)	p Value
Improved global assessment†	30/45 (67%)	75/125 (57%)	106/178 (60%)	NS
Improved NYHA class†	22/35 (63%)	71/106 (67%)	82/140 (59%)	NS
NYHA class III or IV†	14/38 (34%)	71/107 (30%)	62/143 (43%)	= 0.001
6 Month mortality	14/59 (24%)	25/168 (15%)	73/265 (28%)	= 0.01
6 Month cardiac event (AVR or repeat valvuloplasty)	14/59 (24%)	27/168 (16%)	25/265 (9%)	= 0.007
Mean time to last follow-up (all pts.) (mo.)	7.02	7.16	7.22	

*The number of patients varies because there was limited or no assessment in patients who died or underwent cardiac surgery at last follow-up. †At last follow-up. AVR = aortic valve replacement; NYHA = New York Heart Association; other abbreviations as in Table 1.

significant differences among the three groups. Change in valve area and valve area index also did not differ significantly among the three groups.

On average, valve area increased approximately 0.32 cm² and valve gradient decreased approximately 30 mm Hg in these patients. As was the case before valvuloplasty, valve area was significantly inversely correlated with final cardiac index and increasing age ($p < 0.001$).

The occurrence of nonfatal complications was not substantially different among the three groups. These complications and their overall frequency in this patient group are discussed elsewhere in this Seminar. The occurrence of in-hospital death ranged from 4.2% to 9.4% but was not statistically different among the groups.

Outcome at last follow-up (Table 5). The mean duration of follow-up was approximately 7 months; all patients were followed up for at least 6 months. The number of patients who showed improvement at follow-up decreased with age, ranging from 67% in patients <70 to 60% in patients ≥80 years of age (p = NS). Similarly, there was less improvement in functional class in the older patients. However, significantly more patients were in functional class III or IV in the group ≥80 years of age than in the two younger groups ($p = 0.001$). The 6 month mortality rate was highest in patients ≥80 (28%), next highest in patients <70 (24%) and lowest in patients 70 to 79 years of age (15%, $p = 0.011$). Other events recorded at 6 months (aortic valve replacement or repeat valvuloplasty) were least common in patients ≥80 and most common in patients <70 years of age ($p = 0.007$).

Univariate analysis of 20 selected variables demonstrated that only ejection fraction and cardiac output before valvuloplasty were significantly related to mortality at follow-up in all three age groups. Multivariate analysis produced dissimilar discriminant functions for each age group. However, in general, measures of left ventricular function and cardiac output again were important factors in the multivariate analysis.

Discussion

Aortic valvuloplasty has been thought to yield better results in younger patients, probably because there is less severe thickening, calcification and rigidity of aortic cusps. Younger patients also may have a higher prevalence of bicuspid aortic stenosis and rheumatic aortic valve disease in contrast to the senile calcific stenosis seen in older patients. The prevalence of each of these anatomic subtypes remains undetermined in this and all other clinical studies of balloon valvuloplasty.

Immediate results. In this registry study, older patients did have more severe aortic stenosis at baseline assessment of valve area, even after correction for differences in body surface area. However, the incidence of successful valvuloplasty, as assessed by increases in valve area and indexed valve area and a decrease in pressure gradient, was comparable in all three age groups. These results demonstrate that the functional changes produced by balloon valvuloplasty are equivalent in older and younger patients.

It is also clinically important that complications occurred no more frequently in the oldest patients than in patients in the youngest group, and in-hospital mortality rates were also similar in patients <70 years and those ≥80 years of age. This in-hospital mortality rate was still substantial, however, ranging from 8.5% in the youngest group to 9.4% in the oldest.

Follow-up results. At last follow-up, there were more patients in the oldest age group in functional class III or IV as well as a significantly lower mortality rate in the 70 to 79 year old patients (15%) than in the other two groups (24% and 28%, respectively). The reasons for these differences remain uncertain though they could relate to coexistent disease processes. Alternatively, the lower mortality for the middle age group (70 to 79 years) may just be a statistical aberration. Univariate and multivariate analysis of variables possibly related to mortality were performed in an attempt to identify patients at increased risk of death during follow-up. Only left ventricular function and cardiac output emerged as important factors in all age groups. Age alone is probably not an important factor in mortality at follow-up, since the observed mortality rates of 24% to 28% at a mean of 7 months in the youngest (<70 years) and oldest (≥80 years) groups is so much higher than that expected by age alone. Although there was an inverse relation between events at 6 months and age, this relation may

simply reflect the reluctance to perform further procedures in the older age population.

Limitations. Limitations of this study include its observational design and the voluntary nature of the registry, which possibly allowed bias by exclusion of patients at nonparticipating centers. While the relatively modest improvement in valve area is in keeping with most other published data, the use of 23 mm balloons in a larger number of patients might conceivably have resulted in differences in results as applied in the three age groups studied. The trend toward more global (cardiac output and functional class) improvement in younger versus older patients might have reached statistical significance in a larger sample size of patients.

Conclusions. Balloon aortic valvuloplasty remains a palliative procedure with continued high event and mortality rates at short-term follow-up. Somewhat contrary to expectations, older patients have as good results in terms of objective measures of valve area and gradient reduction as do younger patients. Only minimal differences in symptomatic status are found at follow-up; however, mortality remains substantial. The application of balloon aortic valvuloplasty, as performed in this registry study, to younger patients might not be expected to yield substantially better results than those found in older patients.

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